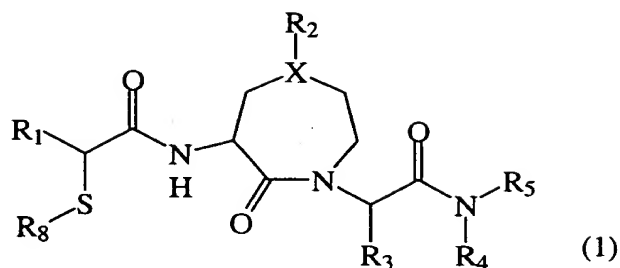


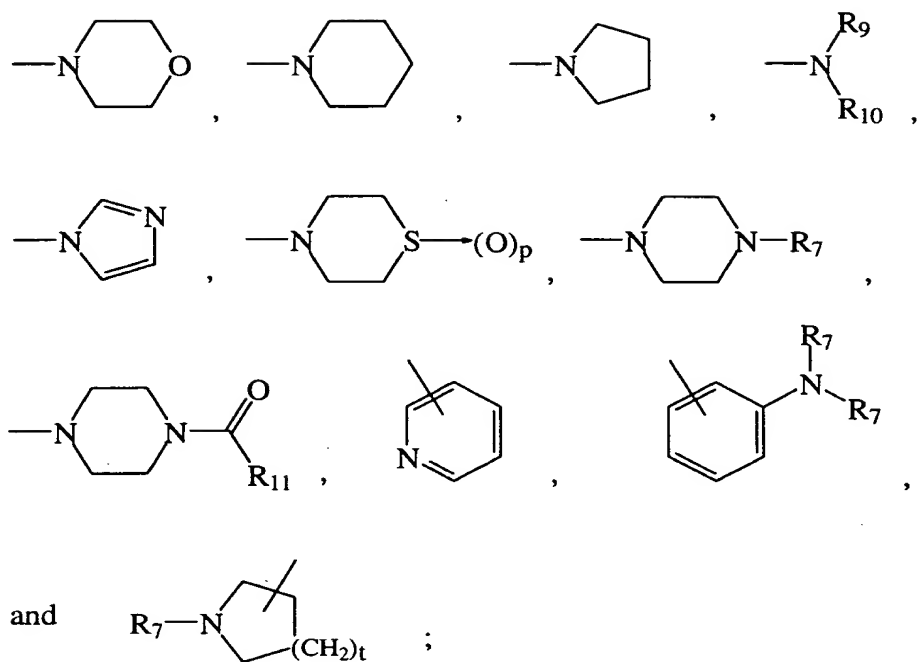
WHAT IS CLAIMED IS:

1. A compound of the formula

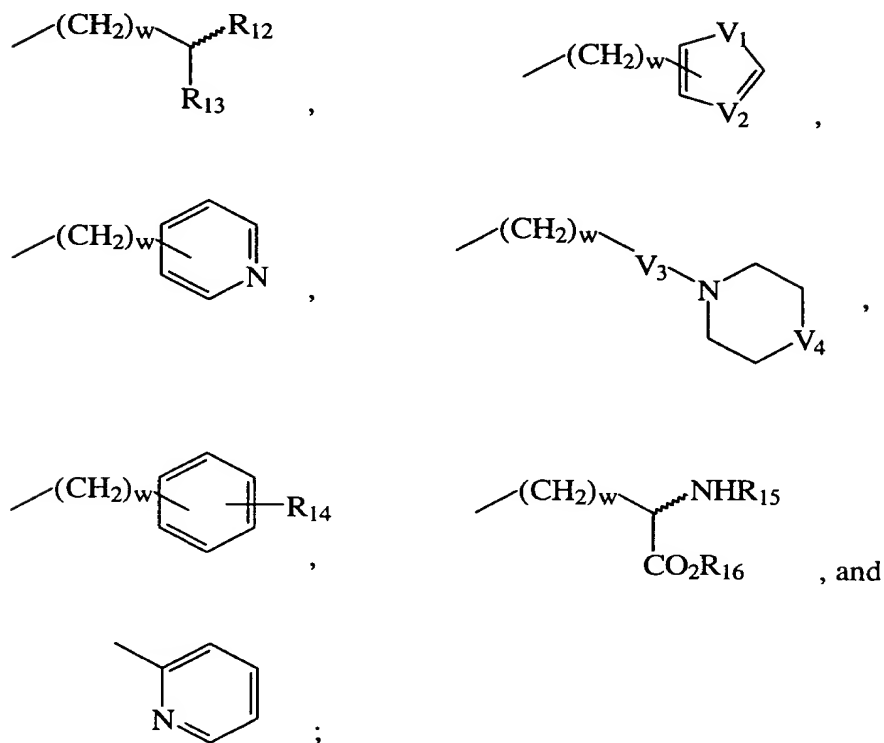


wherein

- R_1 is C_1 - C_6 alkyl, a W -(CH_2) $_m$ - group, or a Q - Z -(CH_2) $_m$ - group wherein W is phthalimido; Z is a bond or is oxy, NR_6 , $C(O)NR_6$, $NR_6C(O)$, $NHC(O)NR_6$, $OC(O)NR_6$, $HNC(O)O$, or SO_2NR_6 ; Q is hydrogen, or a Y -(CH_2) $_n$ - group wherein Y is hydrogen, C_6 - C_{10} aryl, C_3 - C_9 heteroaryl, $-C(O)OR_6$, $-N(R_6)_2$, morpholino, piperidino, pyrrolidino, or isoindolyl;
- R_2 is C_1 - C_4 alkyl, a $-(CH_2)_p$ -(C_3 - C_9)heteroaryl group, or a $-(CH_2)_p$ - Ar_1 group wherein Ar_1 is phenyl or naphthyl optionally substituted with a substituent selected from the group consisting of halogen, C_1 - C_4 alkyl, $-OR_7$, $-N(R_6)_2$, $SO_2N(R_6)_2$ or $-NO_2$;
- R_3 is hydrogen, C_1 - C_6 alkyl, $-CH_2SCH_2NHCOCH_3$, a $-(CH_2)_p$ - A group, a $-(CH_2)_m$ - B group or a $-CH_2$ - D - R_7 group wherein A is C_6 - C_{10} aryl, C_3 - C_9 heteroaryl, or cyclohexyl; B is $-N(R_7)_2$, guanidino, nitroguanidino, $-C(O)OR_6$ or $-C(O)NR_6$; and D is oxy or thio;
- R_4 is hydrogen or a $-(CH_2)_m$ - $S(O)_pX'(R_6)_2$ group;
- R_5 is hydrogen, C_1 - C_6 alkyl or R_4 and R_5 taken together with the nitrogen atom to which they are attached form piperidino, pyrrolidino, or isoindolyl;
- R_6 is hydrogen or C_1 - C_6 alkyl;
- R_7 is hydrogen, C_1 - C_4 alkyl, or a $-(CH_2)_p$ - Ar_2 group wherein Ar_2 is phenyl or naphthyl optionally substituted with a substituent selected from the group consisting of halogen, C_1 - C_4 alkyl, $-OR_7$, $-N(R_6)_2$, $SO_2N(R_6)_2$ or $-NO_2$;
- R_8 is hydrogen, $-C(O)R_7$, a $-C(O)$ -(CH_2) $_q$ - K group or a $-S$ - G group, wherein K is selected from the group consisting of



G is selected from the group consisting of



- 5 R_9 and R_{10} are each independently $\text{C}_1\text{--C}_4$ alkyl or a $\text{---}(\text{CH}_2)_p\text{---Ar}_2$ group;
 R_{11} is ---CF_3 , $\text{C}_1\text{--C}_{10}$ alkyl or a $\text{---}(\text{CH}_2)_p\text{---Ar}_2$ group;

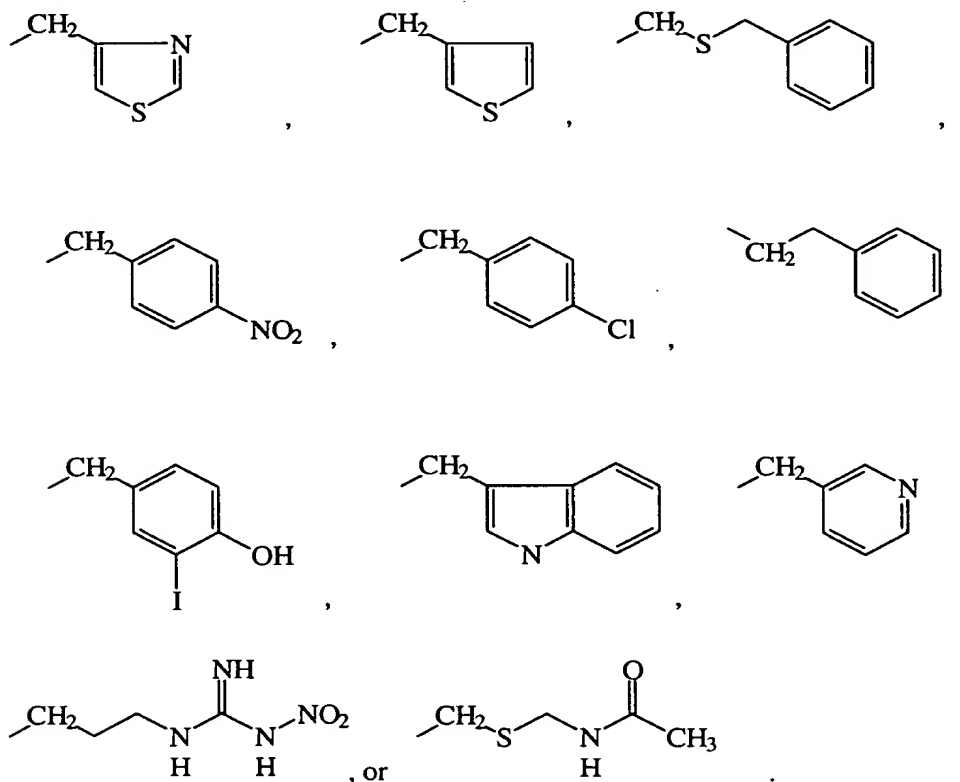
- R_{12} is hydrogen, C_1 - C_6 alkyl, $-CH_2CH_2S(O)_pCH_3$, or arylalkyl;
 R_{13} is hydrogen, hydroxy, amino, C_1 - C_6 alkyl, N-methylamino, N,N-dimethylamino, $-CO_2R_{17}$ or $-OC(O)R_{18}$ wherein R_{17} is hydrogen, $-CH_2O-C(O)C(CH_3)_3$, C_1 - C_4 alkyl, a $-(CH_2)_p-Ar_2$ group or diphenylmethyl and R_{18} is hydrogen, C_1 - C_6 alkyl or phenyl;
 R_{14} is 1 or 2 substituents independently chosen from the group consisting of hydrogen, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, or halogen;
 R_{15} is hydrogen, C_1 - C_6 alkyl or a $-(CH_2)_p-Ar_2$ group;
 R_{16} is hydrogen or C_1 - C_4 alkyl;
 V_1 is O, S, or NH;
 V_2 is N or CH;
 V_3 is a bond or $-C(O)-$;
 V_4 is $-(CH_2)_w-$, O, S, NR_7 , or $NC(O)R_{11}$;
X and X' are each independently CH or N;
m is an integer 2-4;
n is zero or an integer 1-4;
p is zero or an integer 1-2;
q is zero or an integer 1-5;
t is an integer 1-2;
w is an integer 1-3; and
w' is zero or an integer 1; or
a pharmaceutically acceptable salt, stereoisomer or hydrate thereof.

2. A compound of claim 1 wherein X is CH.

3. A compound of claim 2 wherein R_2 is C_1 - C_4 alkyl or a $-(CH_2)_p-Ar$ group wherein Ar is phenyl optionally substituted with F, Cl, C_1 - C_4 alkyl, $-NO_2$, $-NH_2$ or $-OR_7$; and R_4 is hydrogen.

4. A compound of claim 3 wherein R_3 is hydrogen, C_1 - C_6 alkyl, phenyl, benzyl, 1-naphthyl, 2-naphthyl, cyclohexylmethyl, 2-hydroxyphenyl, 3-hydroxyphenyl, 4-hydroxyphenyl, 2,3-dihydroxyphenyl, 2,4-dihydroxyphenyl, 3,4-dihydroxyphenyl, 4-methoxyphenyl, 4-ethoxyphenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 3,4-dichlorophenyl, 4-bromophenyl, 3,4-dibromophenyl, 4-fluorophenyl, 3,4-difluorophenyl, 3-tolyl, 4-tolyl, 4-

ethylphenyl, 4-isopropylphenyl, 3-aminophenyl, 4-aminophenyl, 3,4-diaminophenyl, N-methyl-4-aminophenyl, 2-nitrophenyl, 4-nitrophenyl, 4-aminobenzyl, 4-hydroxybenzyl, 4-methoxybenzyl, 3-chlorobenzyl, 4-fluorobenzyl, 3,4-dichlorobenzyl, 4-bromobenzyl, 4-methylbenzyl, $-\text{CH}_2\text{SCH}_2\text{NHCOCH}_3$, or is a compound of the formula



5. A compound of claim 4 wherein R_5 is hydrogen, methyl, ethyl, propyl, isopropyl, butyl or isobutyl and R_8 is hydrogen.

6. A compound of claim 2 wherein R_1 is a $W-(\text{CH}_2)_m-$ group.

7. A compound of claim 3 wherein R_1 is a $W-(\text{CH}_2)_m-$ group.

8. A compound of claim 5 wherein R_1 is a $W-(\text{CH}_2)_m-$ group.

9. A compound of claim 2 wherein R_1 is C_1-C_6 alkyl.

10. A compound of claim 3 wherein R_1 is C_1-C_6 alkyl.

11. A compound of claim 5 wherein R_1 is a C_1 - C_6 alkyl.

12. A compound of claim 2 wherein R_1 is a $Q-Z-(CH_2)_m$ - group.

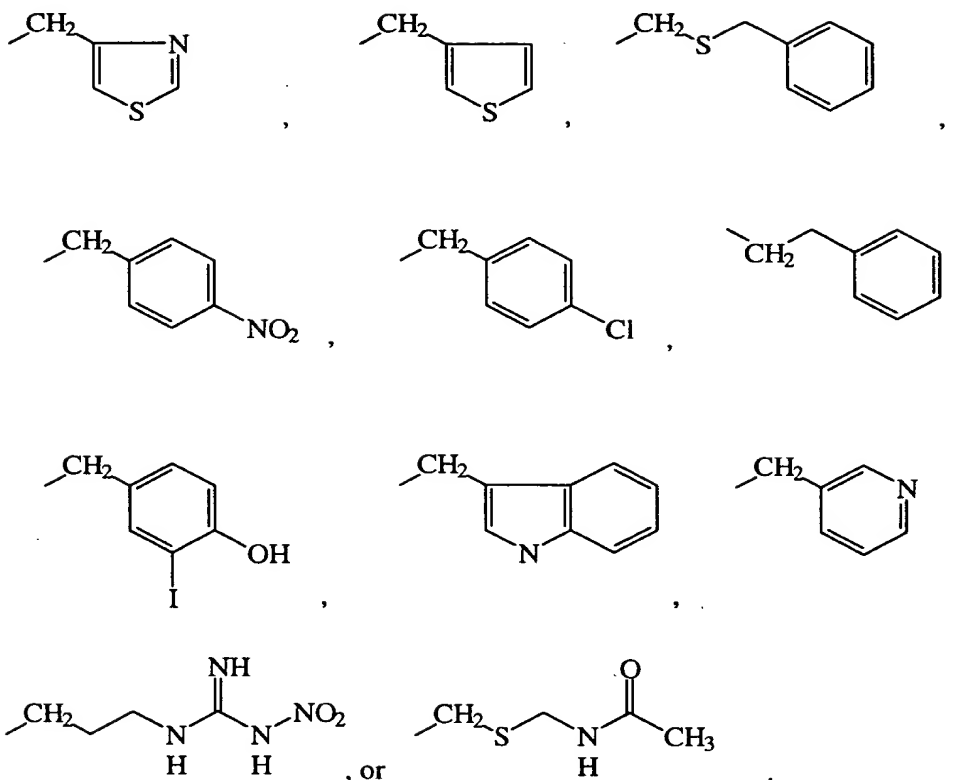
13. A compound of claim 3 wherein R_1 is a $Q-Z-(CH_2)_m$ - group.

14. A compound of claim 5 wherein R_1 is a $Q-Z-(CH_2)_m$ - group.

15. A compound of claim 1 wherein X is N.

16. A compound of claim 15 wherein R_2 is C_1 - C_4 alkyl or a $-(CH_2)_p$ -Ar group wherein Ar is phenyl optionally substituted with F, Cl, C_1 - C_4 alkyl, $-NO_2$, $-NH_2$ or $-OR_8$; and R_4 is hydrogen.

17. A compound of claim 16 wherein R_3 is hydrogen, C_1 - C_6 alkyl, phenyl, benzyl, 1-naphthyl, 2-naphthyl, cyclohexylmethyl, 2-hydroxyphenyl, 3-hydroxyphenyl, 4-hydroxyphenyl, 2,3-dihydroxyphenyl, 2,4-dihydroxyphenyl, 3,4-dihydroxyphenyl, 4-methoxyphenyl, 4-ethoxyphenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 3,4-dichlorophenyl, 4-bromophenyl, 3,4-dibromophenyl, 4-fluorophenyl, 3,4-difluorophenyl, 3-tolyl, 4-tolyl, 4-ethylphenyl, 4-isopropylphenyl, 3-aminophenyl, 4-aminophenyl, 3,4-diaminophenyl, N-methyl-4-aminophenyl, 2-nitrophenyl, 4-nitrophenyl, 4-aminobenzyl, 4-hydroxybenzyl, 4-methoxybenzyl, 3-chlorobenzyl, 4-fluorobenzyl, 3,4-dichlorobenzyl, 4-bromobenzyl, 4-methylbenzyl, $-CH_2SCH_2NHCOCH_3$, or is a compound of the formula



18. A compound of claim 17 wherein R_5 is hydrogen, methyl, ethyl, propyl, isopropyl, butyl or isobutyl and R_8 is hydrogen.

19. A compound of claim 16 wherein R_1 is a $\text{W}-(\text{CH}_2)_m$ - group.

20. A compound of claim 17 wherein R_1 is a $\text{W}-(\text{CH}_2)_m$ - group.

21. A compound of claim 19 wherein R_1 is a $\text{W}-(\text{CH}_2)_m$ - group.

22. A compound of claim 16 wherein R_1 is C_1 - C_6 alkyl.

23. A compound of claim 17 wherein R_1 is C_1 - C_6 alkyl.

24. A compound of claim 19 wherein R_1 is a C_1 - C_6 alkyl.

25. A compound of claim 16 wherein R_1 is a $\text{Q-Z}-(\text{CH}_2)_m$ - group.

26. A compound of claim 17 wherein R_1 is a $Q-Z-(CH_2)_m$ - group.

27. A compound of claim 19 wherein R_1 is a $Q-Z-(CH_2)_m$ - group.

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28. A compound of claim 1 wherein X is CH; R_2 is phenyl, methyl or ethyl; R_3 is phenyl, benzyl, cyclohexylmethyl, isopropyl, isobutyl, 3-pyridylmethyl, 4-fluorobenzyl or 4-aminobenzyl; R_4 is hydrogen; R_5 is hydrogen, methyl, ethyl, propyl, isopropyl, butyl or isobutyl and R_8 is hydrogen.

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29. A compound of claim 28 wherein R_1 is a $W-(CH_2)_m$ - group.

30. A compound of claim 1 wherein X is N; R_2 is phenyl, methyl or ethyl; R_3 is phenyl, benzyl, cyclohexylmethyl, isopropyl, isobutyl, 3-pyridylmethyl, 4-fluorobenzyl or 4-aminobenzyl; R_4 is hydrogen; R_5 is hydrogen, methyl, ethyl, , propyl, isopropyl, butyl or isobutyl and R_8 is hydrogen.

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31. A compound of claim 30 wherein R_1 is a $W-(CH_2)_m$ - group.

32. A compound of claim 1 wherein said compound is 2*H*-Isoindole-2-hexanamide, *N*-[hexahydro-1-[2-(methylamino)-2-oxo-1-(phenylmethyl)ethyl]-2-oxo-5-phenyl-1*H*-azepin-3-yl]-1,3-dihydro- α -mercapto-1,3-dioxo-, [3*S*-[1(*R**), 3 α , 5 α]]-.

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33. A compound of claim 1 wherein said compound is 2*H*-Isoindole-2-hexanamide, *N*-[hexahydro-1-[2-(methylamino)-2-oxo-1-(phenylmethyl)ethyl]-2-oxo-5-phenyl-1*H*-azepin-3-yl]-1,3-dihydro- α -mercapto-1,3-dioxo-, [3*S*-[1(*R**), 3 α , 5 β]]-.

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34. A compound of claim 1 wherein said compound is 2*H*-Isoindole-2-hexanamide, *N*-[hexahydro-4-[2-(methylamino)-2-oxo-1-(phenylmethyl)ethyl]-5-oxo-1-(phenylmethyl)-1*H*-1,4-diazepin-6-yl]-1,3-dihydro- α -mercapto-1,3-dioxo-, [6*S*-[4(*R**), 6*R**(*R**)]]-.

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35. A pharmaceutical composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier.

36. A method of inhibiting matrix metalloproteinase in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

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37. A method of inhibiting MMP-induced tissue disruption and/or MMP-induced tissue degradation in a patient in need thereof which comprises administering to the patient and effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

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38. A method of treating rheumatoid arthritis in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

39. A method of treating osteoarthritis in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

40. A method of treating a chronic inflammatory disorder in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

41. A method of treating a neoplastic disease state in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

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42. A method of treating a cardiovascular disorder in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

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43. A method of claim 42 wherein said cardiovascular disorder is atherosclerosis.

44. A method of treating corneal ulceration in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

45. A method of treating gingivitis or periodontal disease in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

46. A method of treating multiple sclerosis in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

47. A method of treating chronic obstructive pulmonary disorder in a patient in need thereof which comprises administering to the patient an effective matrix metalloproteinase inhibiting amount of a compound of claim 1.

[illegible]